P960042

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Mr. Michael J. Quinn
Director, Regulatory Affairs
Spectranetics Corporation
96 Talamine Court
Colorado Springs, Colorado 80907-5159

DEC - 9 1997

Re: P960042
12 French Laser Sheath Kit
Filed: November 26, 1996
Amended: April 7, May 22, June 11 and 23, July 18, August 18, September 24 and 29, and December 9, 1997

Dear Mr. Quinn:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the 12 French Laser Sheath Kit which consists of the 12 French Laser Sheath (Model 500-001) and Fish Tape accessory. The device is indicated for use as an adjunct to conventional lead extraction tools in patients suitable for transvenous removal of chronically implanted pacing or defibrillator leads constructed with silicone or polyurethane outer insulation. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the results of a post-approval study of the initial clinical experience of the 12 French Laser Sheath. The study should be conducted at all sites where the device is used upon PMA approval and include data on the first ten patients treated at each site. The data collected for each patient should be similar to those collected during the clinical trial of the Laser Sheath (e.g., patient and lead demographical information, indications for lead removal, acute procedural outcome data). These data will be used to determine the "learning curve" of device use by physicians who may

not be experienced in lead extraction techniques and whether revisions to the physician training requirements need to be made. The study should continue for two years after PMA approval. Periodic reports of this information should be submitted to the PMA at 6-month intervals.

Expiration dating for this device has been established and approved at two years.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

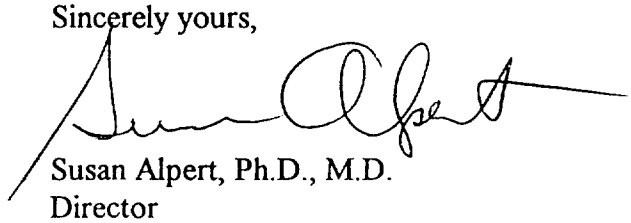
You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Christopher M. Sloan at (301) 443-8243.

Sincerely yours,



Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

SUMMARY of SAFETY and EFFECTIVENESS DATA

Spectranetics 12 French Laser Sheath Kit

Table of Contents

SUMMARY of SAFETY and EFFECTIVENESS DATA

1. GENERAL INFORMATION

Device Generic Name: ..... Pacemaker Lead Removal Device

Device Trade Name: ..... Spectranetics 12 French Laser Sheath Kit

Applicant's Name and Address:..... Spectranetics Corporation
96 Talamine Court
Colorado Springs, CO 80907

PMA Application Number: P960042

Date of Panel Recommendation:..... July 29, 1997

Date of Notice of Approval to the Applicant: ..December 9, 1997

2. INTENDED USE/INDICATIONS

The Laser Sheath is intended for use as an adjunct to conventional lead extraction tools in patients suitable for transvenous removal of chronically implanted pacing or defibrillator leads constructed with silicone or polyurethane outer insulation.

3. CONTRAINDICATIONS

Use of the Laser Sheath is contraindicated:

- When emergency thoracotomy with cardiopulmonary bypass can not be performed immediately in the event of a life threatening complication;
- When fluoroscopy is not available;
- In patients in whom the superior venous approach cannot be used;
- When the proximal end of the pacing lead is not accessible to the operator;
- When the lead will not fit into the inner lumen of the laser sheath.

4. WARNINGS and PRECAUTIONS

See the attached final draft labeling.

5. DEVICE DESCRIPTION

The Spectranetics 12 Fr. Laser Sheath Kit includes a 12 Fr. Laser Sheath and a Fish Tape. The Laser Sheath is an intra-operative device used to free chronically implanted pacing or defibrillator lead.

The Laser Sheath consists of optical fibers arranged in a circle, sandwiched between inner and outer polymer tubing. The fibers terminate at the distal end within a polished tip and at the proximal end within the coupler that mates with the excimer laser system. At the distal tip, the

fibers are protected by inner and outer stainless steel bands, which form a radiopaque marker. The inner lumen of the device is designed to allow a pacing lead to pass through it, as the device slides over the lead towards the tip of the lead in the heart.

The Laser Sheath is designed for use only with the Spectranetics CVX-300® Excimer Laser System which was approved under P910001. The multifiber laser sheaths transmit ultraviolet energy from the Spectranetics CVX-300® laser to the tissue at the distal tip of the device. When the laser fires, a small amount of the tissue is ablated, thereby freeing the lead from overgrowth in a controllable fashion.

The Laser Sheath is used in conjunction with conventional lead extraction tools (e.g., locking stylets, outer sheaths).

The Fish Tape is an accessory to assist in the loading of the Laser Sheath over an implanted lead. The Fish Tape is a 60 cm long, 0.024" diameter, stainless steel mandrel with a wire loop handle on one end and a closed wire hook on the other end.

Figure 5-1. Spectranetics 12 Fr. Laser Sheath

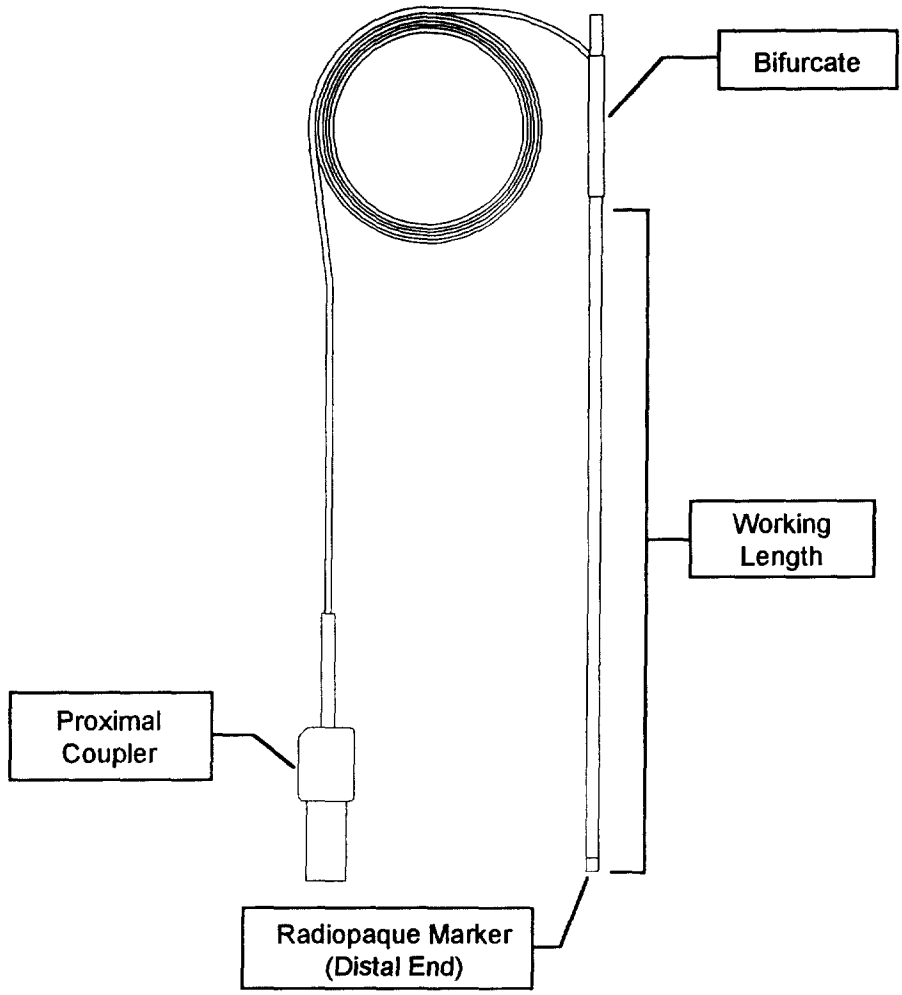
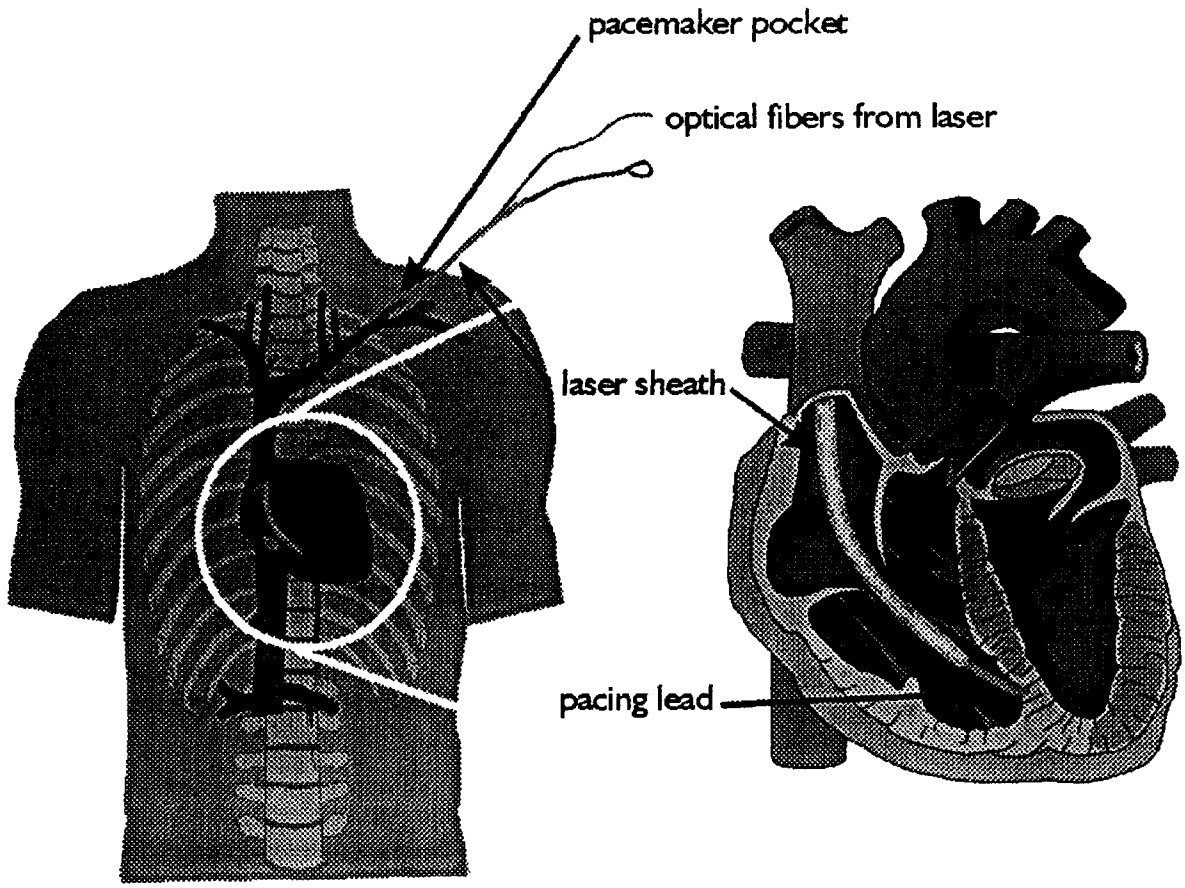


Figure 5-2. Spectranetics 12 Fr. Laser Sheath in Use



6. ALTERNATIVE PRACTICES AND PROCEDURES

Traction

Pulling on leads (traction) was a successful method of extracting leads during the early years of pacing, when leads lacked efficient fixation devices and were implanted for short periods of time. Traction had a high incidence of failure and other complications when applied to leads with efficient fixation devices or those implanted for longer periods of time. The amount of traction required for lead extraction increases as the duration of the implant and the tensile strength of the fibrous overgrowth tissue increases.

Leads with efficient passive fixation devices may be difficult to remove four or more months after implantation. Complications include low cardiac output, lead breakage and migration, avulsion of veins and myocardial tissue (e.g., muscle, tricuspid valve) and tears of the veins and heart wall with possible hemothorax, tamponade, and/or death.

Intravascular Countertraction

Intravascular countertraction is defined as the countering of the traction on the lead by a sheath. A sheath of slightly larger diameter is passed over the lead to a point approximately 1 cm from the right atrium wall or right ventricle wall (heart wall). Countertraction applied to the heart wall at the electrode-myocardial interface focuses the force perpendicular to the heart wall. Since only scar tissue is present between the sheath and the heart wall, cardiac tissue is not generally in jeopardy. The amount of traction applied to the lead is limited only by the tensile strength of the lead. By countering the traction, the remainder of the heart wall is not subject to this force. Once sufficient traction is applied, the electrode is removed from the scar tissue at the electrode-myocardial interface and pulled up into the lumen of the sheath. When the electrode breaks free, the stationary countertraction sheath remains in the ventricular or atrial cavity and is no longer in contact with the heart wall.

Passage of the sheaths over the lead and down to the electrode is a prerequisite to applying countertraction. To reach a point near the electrode, the sheaths must pass through the fibrous tissue binding sites along the venous tract and heart wall. The force applied to the fibrous tissue binding sites at the venous entry point and along the venous tract and heart wall fundamentally differs from the countertraction as applied at the electrode-myocardial interface. The sheath is pushed into the vein against the fibrous tissue at the binding site, creating pressure. Intravascular counterpressure is the pressure applied by the sheath to the tissue at a binding site countered by the tissue resistance. The tissue resistance countering this pressure is a combination of the tensile strength of the fibrous tissue binding the lead and the strength of the vein or heart wall. The same sheaths are used for applying counterpressure at the binding sites along the lead and for applying countertraction at the electrode-myocardial interface.

Counterpressure provides a shearing force to release the lead. Properly applied, it stretches and tears the fibrous tissue or shears it off the lead. If, however, an excessive shearing force is applied, a misdirected tear can create a dissection, false lumen or perforation, tearing the vein or heart wall. Training, judgment and experience are particularly important in safe lead removal.[1]

Passage of sheaths along the circuitous route down the lead to the heart is successful for most leads. However, leads implanted for greater than three months have an increasing incidence of failure to extract due to the tensile strength of the scar tissue.[2]

IVC, SVC, and Transtrial Approaches to Lead Removal

A series of transvenous and thoracic surgical procedures have evolved using countertraction techniques. Countertraction extraction approaches include the superior vena cava (SVC), the inferior vena cava (IVC), and the transatrial (TA). The majority of leads can be removed using the transvenous SVC and IVC approaches individually or in combination. The IVC approach is the procedure of choice for broken or cut leads free floating in the veins, heart or pulmonary artery, and for leads passing through occluded veins. The IVC approach is also used for failures of a SVC approach. In some situations, both the SVC and IVC approaches fail and countertraction is applied through a TA approach using a small anterior thoracotomy.

The SVC approach is the initial approach used by most physicians[1,3]. The SVC approach combines the pocket abandonment procedure with passage of the dilator sheaths to the electrode.

In all cases, the leads are exposed, debrided of inflammatory tissue, and freed from restraining sutures as part of the abandonment procedure. A locking stylet is passed through the central lumen of the lead to the electrode and locked. Stainless steel sheaths are required to break through the scar tissue at the vein entry site. A telescoping set of rigid stainless steel sheaths is used. These sheaths are passed over the lead in the subcutaneous tissue and used to break through the tissue at the vein entry site. The tissue at the vein entry site ranges from fibrous tissue capsule, of varying tensile strength, to bone. These sheaths were designed to allow a sufficient longitudinal force to be applied to break just into the vein.

Once inside the vein, the stainless steel sheaths are exchanged for the flexible plastic telescoping sheaths which are for maneuvering around curves and forcing through the circumferential bands of fibrous tissue. Sufficient traction is applied to support the smaller supple sheath for maneuvering around curves in the vein. The smaller sheath then acts as a guide, supporting the advancement of the larger, more rigid outer sheath. Fluoroscopic visualization is essential to avoid creating a false passage, tearing the vein or heart wall.

7. MARKETING HISTORY

The 12 Fr. Laser Sheath has not been marketed in the United States or any foreign country.

8. ADVERSE EVENTS

Patients with indications for lead removal (N=301) and with the targeted lead implanted at least one year prior were randomly assigned into the LASER or NonLASER groups in nine US centers. These 301 patients (465 leads) form the basis for the adverse events reporting.

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8.1 Observed Adverse Events

Table 8-1. Acute Complications and Complications at 1-month

All patients randomized (N=301)

	LASER (N=153)		Non-LASER (N=148)		TOTAL (N=301)	
Complications - Acute	**n**	**%**	**n**	**%**	**n**	**%**
Perioperative Death	1	0.65%	0	0	1	0.3%
Hemopericardium tamponade	2	1.3%	0	0	2	0.7%
Hemothorax	1	0.65%	0	0	1	0.3%
Complications - One month	**LASER (N=145)**		**Non-LASER (N=140)**		**TOTAL (N=285)**	
Death	2	1.4%	1	0.7%	3	1.1%
Complications - any one or more	4	2.8%	3	2.1%	7	2.5%
Pain at cut-down site	1	0.7%	0	0.0%	1	0.4%
Arm swelling	1	0.7%	1	0.7%	2	0.7%
Infection	1	0.7%	1	0.7%	2	0.7%
SVC thrombosis	0	0.0%	1	0.7%	1	0.4%
Tricuspid regurgitation	1	0.7%	0	0.0%	1	0.4%

8.2 Potential Adverse Events

The following adverse events or conditions may also occur during lead extraction with the Laser Sheath, but were not observed during the clinical study (listed in alphabetical order):

- bacteremia
- low cardiac output
- migration of lead fragments
- migration of vegetation
- myocardial avulsion
- perforation
- premature ventricular contractions
- pulmonary embolism
- stroke
- venous avulsion
- ventricular tachycardia

9. SUMMARY OF PRE-CLINICAL STUDIES

9.1 Biocompatibility Testing

Laser Sheath Biocompatibility

All patient-contacting materials used in the 12 Fr. Laser Sheath, except the distal jacket material (polyolefin shrink tubing), are identical to those used in PMA-approved Spectranetics laser angioplasty catheters (P910001). These catheter materials have previously been shown to be safe

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for human use based on biocompatibility testing conducted in accordance with the *Tripartite Biocompatibility Guidance for Medical Devices*. This prior testing is applicable to the Laser Sheath given the similarities in manufacturing and sterilization processes between the Laser Sheath and the laser angioplasty catheters.

The biocompatibility of the distal jacket (final, sterilized component) was evaluated separately. This component passed the following tests with acceptable results: subchronic (14-day) toxicity, sensitization, cytotoxicity, material-mediated pyrogenicity, hemolysis, thrombogenicity and mutagenicity. "White" tubing, which includes a white colorant, was actually tested. However, data are applicable to the "natural color" tubing used in the device since it is identical to the white tubing except for the absence of the colorant. The material supplier certified that the material also passed USP Class VI testing (irritation, acute systemic toxicity, and implantation tests). The testing conducted supports the biocompatibility of the distal jacket material (polyolefin shrink tubing). In conclusion, the above referenced biocompatibility information shows that the patient-contacting materials used in the Laser Sheath are safe for their intended use.

Lead Insulation Biocompatibility and Particulate Testing (Lased Silicone and Polyurethane)

Additional biocompatibility testing was conducted on common pacing and defibrillator lead insulation materials (i.e., polyurethane and silicone) which had been lased by the Laser Sheath. These tests were performed to examine if laser energy (60 fluence at 40 Hz for a train of 200 pulses) caused any chemical or physical changes in the insulation that affected its biocompatibility. Lased polyurethane and silicone insulation from pacing leads were evaluated with the following biocompatibility tests with acceptable results: sensitization, irritation, systemic toxicity, cytotoxicity, hemolysis, and thrombogenicity. The test battery was designed to evaluate the biocompatibility of a short-term, blood-contacting material since the purpose of the Laser Sheath procedure is remove the lead immediately upon freeing it from the vasculature. The results show that the insulation materials remain biocompatible following exposure to laser energy.

Testing was also conducted to survey the amount and composition of particles generated via direct lasing of polyurethane and silicone lead insulation materials. The number of particles shed from the insulation met the limits established for large volume injections in USP XXIII [section <788>]. Trace chemical analyses of particulates showed that laser exposure of silicone insulation did not produce concentrations of chemical species (i.e., cations, anions or organic molecules) in excess of the control (non-lased sample). Lasing of polyurethane insulation produced a slightly elevated amount of iron in the test sample. The potential patient dose due to laser exposure of polyurethane-insulated leads was calculated to be about 8 micrograms, an amount which is not expected to cause any adverse reactions. Based on the above testing, the particulates generated from lead insulation materials exposed to laser energy transmitted by the Laser Sheath are not expected to cause any untoward effects.

9.2 Bench Testing

A series of bench tests was conducted to evaluate the functionality and reliability of the 12 Fr. Laser Sheath. The test plan was based on a Failure Mode Effects and Criticality Analysis (FMECA) for the device which included a description of all possible failure modes along with their severity and likelihood of occurrence. The tests performed evaluated the susceptibility of the

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device to each of these failure modes. All of the tests discussed below were not performed on the final device design that was studied clinically. Some tests were conducted with a slightly larger 13 Fr. device and others with earlier versions of the 12 Fr. device. However, all individual design elements that are represented in the final device were evaluated during the development of the Laser Sheath. The results of the following tests support the functionality and reliability of the 12 Fr. Laser Sheath for its intended use.

Mechanical Testing of Distal Tip

Four tests were conducted to evaluate the mechanical integrity of the distal tip of the device: outer jacket to outer band bond and fiber to tip epoxy bond (following bending three times over a 3" radius), inner lumen to inner band bond, inner band to tip epoxy bond, and outer band to tip epoxy bond. All samples passed the outer jacket to outer band bond test (i.e., no bond delamination noted upon visual inspection). All samples passed the remaining three pull tests (i.e., bond strengths exceeded expected clinical loads).

Track Testing in Heart Model

The handling (trackability, pushability, and flexibility) of the device was evaluated in an anatomical heart model. Devices were inserted over a pacing lead which was placed around the aortic arch of the model. Ease of movement of the device over the lead and degree of damage to the Laser Sheath subsequent to repeated tracking over the lead were both judged to be acceptable.

Tissue Cutting/Tip Integrity Performance

The ability of the device to ablate (lase) through a tissue sample (porcine aorta) was assessed at a setting of 50 fluence with a 5 gram perpendicular force applied. The ablation rate for two devices (0.9 and 1.7 micron/pulse, respectively) was less than that for a currently marketed excimer laser coronary angioplasty catheter. However, this was not unexpected due to the large dead space at the center of the Laser Sheath. Despite the slow cutting rate, clean cuts through the tissue were noted where active fibers were present. In addition, tip integrity was assessed following lasing (1000 pulses at 60 fluence and 40 Hz) with a 5 gram perpendicular force applied against porcine aorta and bone tissue samples. Pitting and erosion damage of the tip, consistent with that of existing laser angioplasty catheters following similar testing, was noted and judged to be acceptable.

A series of tests (radius bend, kink, tangential ablation, normal ablation, and post-kink lasing tests) was conducted to elicit several possible failure modes of the device and to determine the degree of damage that could occur during these failures. It was noted that fibers may be broken by kinking the device; however, broken fibers do not damage other fibers and do not protrude from the device under expected clinical use conditions. A single fiber when oriented perpendicularly to the surface of the outer tubing was able to ablate through the tubing after 1450 laser pulses at a fluence of 50. The probability of encountering this failure mode clinically is remote.

Radiopacity

The radiopacity of the device (i.e., visualization of marker bands at distal tip) was judged to be acceptable under fluoroscopy.

Shelf Life

Product stability testing performed for the Laser Sheath demonstrated that the sterility and functionality of the device could be maintained for a minimum of two years. Based on these results, the Laser Sheath will be labeled with a 2-year shelf life date.

9.3 Animal Studies

Animal studies were conducted to evaluate the feasibility of removing chronically implanted pacing leads with an excimer laser and laser catheter delivery system. Eight canines each having been implanted with at least one endocardial pacing lead for one year or more were studied. There were three objectives of the animal studies:

1) To test the catheter designs in dogs having chronically implanted leads.

2) To observe any acute effects on the heart and vasculature due to lasing in dogs.

3) To provide experience in laser extraction for physicians already experienced in pacing and lead extraction with conventional tools.

Preparation for each procedure included standard surgical prep and shaving, general anesthesia, and cutdown to expose the venous entry site. The pacing lead connector is cut off and the cut end of the lead body is placed into the lumen of the laser catheter. The laser catheter presents a single row of fiber-optic fiber ends side-by-side in a ring around the lead body. The catheter is advanced into the venotomy site and along the lead body to the tip. When obstruction to catheter advancement along the lead body is encountered, the laser is turned on and "cuts" through obstructive scar tissue by ablating the tissue. The catheter is advanced until its tip is near the distal lead tip, as seen on fluoroscopy. Traction can then be used to free the lead tip from the remaining fibrosis. The lead, still partially coated with a thin layer of fibrotic tissue, and the laser catheter are then removed from the dog. The incisions are ligated, and the animals are allowed to recover with sedation and analgesics. After 24-48 hours, the animals are terminated and necropsy is performed by a veterinary pathologist.

The device designs tested in the first seven canines consisted of monorail designs in which only the distal 1.5-3.0 cm of the device traveled over the lead body. Subsequent to observations of fiber damage and gouging of the insulation in the first two canines, a metal inner band was added the design evaluated in canines #3 and #4. The band prevented the fibers from lasing into the lead and causing insulation damage. Exchangeable stiffening stylets were added to the device designs tested in canines #5 through #7 to offer greater pushability to the catheter. Necropsy revealed intimal damage to the superior vena cava in one canine, but no cases of vessel wall perforation were noted.

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Based on the suggestions made by physicians experienced in lead extraction who used the monorail design in canines #5 through #7, the laser catheter was redesigned to resemble the laser sheath studied clinically. This coaxial laser sheath, in which the lumen runs the entire length of the device (20") rather than only the distal 1.5-3.0 cm, was used in canine #8. The device was used in conjunction with conventional extraction tools (i.e., a Teflon outer sheath which telescoped over the laser sheath and a locking stylet inserted into the lead to apply traction). Two leads were removed from the canine successfully. Minor damage to the lead insulation (i.e., a laser burn on one lead and a nick on the second), outer sheath (i.e., small black spots where the laser impinged on the sheath) and laser sheaths (i.e., pitting of fiber faces, two inactive fibers in one device) were noted. There were no adverse findings at necropsy. Histopathology revealed no untoward changes in tissue sections taken along the tracks of the explanted leads, except for minimal fresh, focal hemorrhages, an expected result of the extraction procedure.

Necropsy revealed no collateral tissue damage attributable to laser irradiation and no overheating of tissue. None of the animals developed complications such as pulmonary embolism, hemothorax or cardiac tamponade. There were no incidents of perforation of a vessel wall. The animal studies established the feasibility of removing chronically implanted pacing leads with an excimer laser and laser catheter delivery system and justified initiation of human clinical evaluation of the device.

10. SUMMARY OF CLINICAL STUDIES

The use of standard tools (NonLASER) only (locking stylets, polymer and stainless steel sheaths, grips, snares, etc.) to explant chronically implanted pacing and defibrillator leads was compared to standard tools plus the 12 Fr. Laser Sheath (LASER). The primary effectiveness measure was the proportion of complete extractions (on a per lead basis). The primary safety measure was complication rate (on a per patient basis).

10.1 Methods

In a typical lead extraction procedure prior to the advent of the laser sheath, the lead was disconnected from the generator and the connector severed. A locking stylet was then placed in the lead. A polymer outer sheath was preloaded over an inner polymer sheath before the stylet and lead were threaded through the assembly. The sheaths were passed over the lead body until the first binding site was reached, whereupon the physician then manipulated the sheaths to tear or dilate the fibrotic invtravascular tissue away from the lead body. The sheath assembly was advanced over the lead until it was freed from its attachments or until the sheath tip reached a point a few millimeters from the heart wall. In the latter case, the outer sheath was advanced to the heart wall and countertraction applied to remove the lead (pushing on the outer sheath while pulling on the lead).

The laser sheath replaces the inner sheath of a telescoping polymer sheath set. The 35 cm long laser sheath consists of thin inner and outer polymer walls, between which a single layer of optical fibers has been spirally wrapped. At the distal tip of the sheath, the fibers present a single circumferential ring of light sandwiched between the inner and outer walls of the tip. At the proximal end of the sheath the fibers pass through a connecting cable to the CVX-300 laser. The

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12 Fr. laser sheath has an inner diameter of 8.3 Fr. (2.8 mm) and an outer diameter of 12.4 Fr. (4.1 mm).

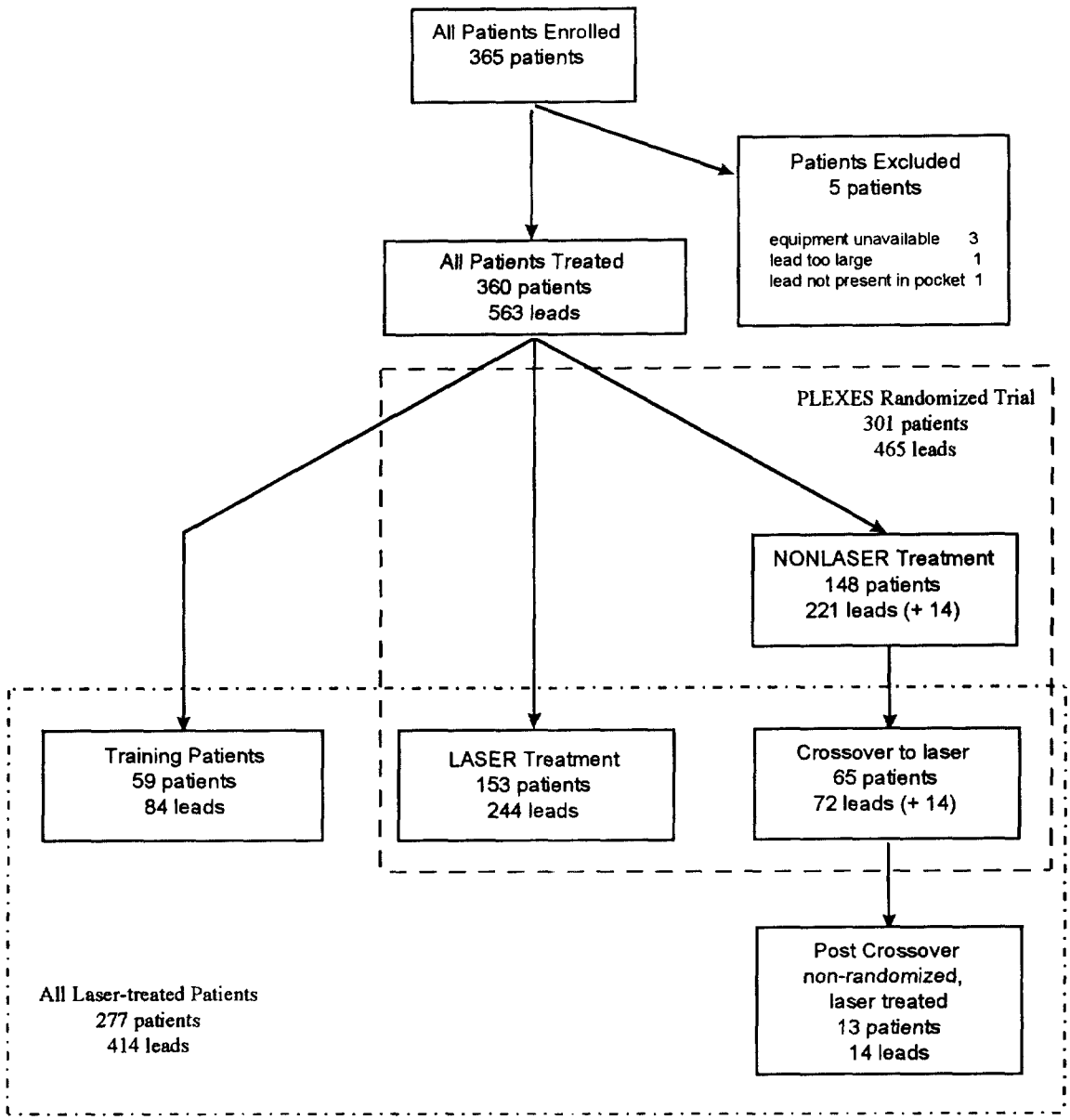
The CVX-300 Excimer XeCl Laser System emits 135 ns pulses (308 nm wavelength) at a repetition rate of 25 - 40 Hz. The fluence (output energy per unit area of fiber) at the distal tip of the device can be set to values between 30 and 60 mJ/mm^2. Settings for this study were 60 mJ/mm^2 and 40 Hz.

The laser-tissue interaction consists of a combination of photochemolysis and photothermal ablation, which causes the layer of tissue immediately in contact with the device tip to disintegrate into particles no larger than 5 microns in diameter. Since the penetration depth of 308 nm light in vascular tissue is less than 100 microns, the laser light is completely absorbed by the tissue immediately in front of the tip. This produces a controlled removal of encapsulating fibrous tissue directly surrounding the lead body and in contact with the tip of the laser sheath.

10.2 Description of Patients and Gender Bias Analysis

A total of 365 patients were enrolled in the clinical study. Five patients were found to meet exclusion criteria after enrollment and were disqualified from the study before any treatment was administered. Thus, 360 patients presented with indications for lead removal and were treated. Of these, 59 were enrolled for investigator training (nonrandomized patients). The remaining 301 patients (with 465 leads) comprised the randomized patients [PLEXES Randomized Trial: **P**acing **L**ead **Ex**traction with the **E**xcimer Laser **S**heath]. Mean patient age was 65 years (range 5 to 94) with 36% females and mean implant duration of 67 months (range 1 to 286). Figure 10-1 shows the Patient Flow and Lead Flow in the clinical study and Table 10-1 shows patient enrollment by site.

Figure 10-1. Patient Flow (n=365) and Lead Flow (n=563)



PATIENT Cohort Definitions

All Patients Treated, N=360
All Laser-treated Patients, N=277
All Patients Randomized, N=301
Training Patients, N=59
LASER Patients, N=153
NonLASER Patients, N=148
Crossover Patients, N=65
Post-Crossover Patients, N=13

LEAD Cohort Definitions

All Leads Treated, N=563
All Laser-treated Leads, N=414
All Leads Randomized, N=465
Training Leads, N=84
LASER leads, N=244
NonLASER Leads, N=221
Crossover Leads, N=72
Post-Crossover Leads, N=14

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Table 10-1. Patient Enrollment by Site

All Patients Treated (n=360) and All Leads Treated {n=563}

Investigator	Center, Location	NonLaser	LASER	Training	Post-Crosso	Total
Byrd	Broward General M.C., FL	50 {63}	51 {91}	27 {39}	10 {11}	128 {204}
Wilkoff	Cleveland Clinic, OH	31 {57}	35 {56}	2 {6}	0 {0}	68 {119}
Love	Ohio State Univ. H.C., OH	24 {42}	25 {36}	8 {10}	0 {0}	57 {88}
Hayes	Mayo Clinic, MN	20 {29}	17 {23}	2 {2}	0 {0}	39 {54}
Sellers	Memorial Hospital, CO	8 {10}	8 {11}	2 {2}	2 {2}	18 {25}
Schaerf	St. Joseph's M.C., CA	7 {10}	7 {11}	3 {5}	0 {0}	17 {26}
Parsonnet	Newark Beth Israel M.C., NJ	4 {4}	4 {7}	2 {3}	0 {0}	10 {14}
Epstein	Beth Israel, Boston, MA	3 {4}	5 {7}	2 {3}	1 {1}	10 {15}
Sorrentino	Duke Univ. M.C., NC	1 {2}	1 {2}	2 {3}	0 {0}	4 {7}
Hoover	Mercy Hospital Center, PA	0 {0}	0 {0}	1 {2}	0 {0}	1 {2}
Kawanishi	Univ. S. Calif. M.C., CA	0 {0}	0 {0}	4 {5}	0 {0}	4 {5}
Brinker	Johns Hopkins M.C., MD	0 {0}	0 {0}	2 {2}	0 {0}	2 {2}
Trantham	Sacred Heart H.C., FL	0 {0}	0 {0}	2 {2}	0 {0}	2 {2}
	Total	148 {221}	153 {244}	59 {84}	13 {14}	360 {563}

Table 10-2 describes the patients and Table 10-3 describes the leads.

Table 10-2. Description of Patients

Number (N) and % of total, or mean ± SD (range), All Patients Randomized (n=301)

	LASER	NonLASER	Total	Diff[95% CI]
Patients (cases)	153	148	301	
Gender:				
Female	51 (33%)	56 (38%)	107 (36%)	-4.5% [-15.3%, 6.3%]
Male	102 (67%)	92 (62%)	194 (64%)	4.5% [-6.3%, 15.3%]
Age, years mean sd(range)	65±18(5,94)	66±18(12,93	65±17(5,94)	-0.4 [-5.8, 5.0]
Indications by Case (see note)				
Mandatory	19 (12%)	16 (11%)	35 (12%)	1.6% [-5.6%, 8.8%]
Septicemia	15 (10%)	12 (8%)	27 (9%)	1.7% [-4.7%, 8.1%]
Endocarditis	7 (5%)	4 (3%)	11 (4%)	1.9% [-2.3%, 6.1%]
Lead Migration	1 (1%)	0	1 (0%)	0.7% [-0.6%, 1.9%]
Device Interference	0	3 (2%)	3 (1%)	-2.0% [-4.3%, 0.2%]
Obliteration of all Usable Veins	2 (1%)	1 (1%)	3 (1%)	0.6% [-1.6%, 2.9%]
Necessary	147 (96%)	140 (95%)	287 (95%)	1.5% [-3.3%, 6.3%]
Pocket Infection	37 (24%)	38 (26%)	75 (25%)	-1.5% [-11.3%, 8.3%]
Chronic Draining Sinus	11 (7%)	9 (6%)	20 (7%)	1.1% [-4.5%, 6.7%]
Erosion	12 (8%)	14 (9%)	26 (9%)	-1.6% [-8.0%, 4.7%]
Vein Thrombosis	8 (5%)	5 (3%)	13 (4%)	1.9% [-2.7%, 6.4%]
Lead Migration	1 (1%)	2 (1%)	3 (1%)	-0.7% [-3.0%, 1.6%]
Potential Device Interference	13 (8%)	26 (18%)	39 (13%)	-9.1%* [-16.6%, -1.5%]
Tricuspid Regurgitation	4 (3%)	3 (2%)	7 (2%)	0.6% [-2.8%, 4.0%]
Lead Replacement	110 (72%)	101 (68%)	211 (70%)	3.7% [-6.7%, 14.0%]
Non-functional	58	48	106	5.5% [-5.3%, 16.2%]
Incompatibility w/ ICDs	2	4	6	-1.4% [-4.6%, 1.8%]
Patient Morbidity	59	47	106	6.8% [-4.0%, 17.6%]

NOTE: Patients may have multiple indications for lead removal.

** Difference statistically significant ($p<0.05$) by Chi square*

Table 10-3. Description of Leads

All Leads Randomized (n=465)

	LASER	NonLASER	Total	Diff. [95%CI]
Leads	244	221	465	
Implant Duration*				
<12 months	4 (2%)	10 (5%)	14 (3%)	-2.9% [-6.1%, 0.3%]
12 - 51 months	98 (40%)	72 (33%)	170 (37%)	7.6% [-1.1%, 16.3%]
52 - 91 months	86 (35%)	86 (39%)	172 (37%)	-3.7% [12.5%, 5.1%]
92 months - 11 years	23 (9%)	26 (12%)	49 (11%)	-2.3% [-7.9%, 3.3%]
11+ years	19 (8%)	21 (10%)	40 (9%)	-1.7% [-6.8%, 3.4%]
Duration of lead implant (mos) mean ± SD (range)	65±42(1,286)	69±46(3,255)	67±44(1,286)	-4.4 [-12.4, 3.6]
Location				
Ventricle	118 (48%)	101 (46%)	219 (47%)	2.7% [-6.4%, 11.7%]
Atrium	125 (51%)	119 (54%)	244 (52%)	-2.6% [11.7%, 6.5%]
Coronary Sinus	1 (0%)	1 (0%)	2 (0%)	
Fixation	n %	n %	n %	
Active	103 (42%)	98 (44%)	201 (43%)	-2.1% [11.1%, 6.9%]
Passive	129 (53%)	109 (49%)	238 (51%)	3.5% [-5.5%, 12.6%]
Unknown/none	12 (5%)	14 (6%)	26 (6%)	-1.4% [-5.6%, 2.8%]
Lead Manufacturer	n %	n %	n %	
Biotronik	1 (0%)	0 (0%)	1 (0%)	
Cordis	8 (3%)	7 (3%)	15 (3%)	0.1% [-3.1%, 3.3%]
CPI	18 (7%)	17 (8%)	35 (8%)	-0.3% [-5.1%, 4.5%]
Daig	0 (0%)	1 (0%)	1 (0%)	
Intermedics	15 (6%)	12 (5%)	27 (6%)	0.7% [-3.5%, 5.0%]
Medtronic	65 (27%)	60 (27%)	125 (27%)	-0.5% [-8.6%, 7.6%]
Oscor	13 (5%)	16 (7%)	29 (6%)	-1.9% [-6.3%, 2.5%]
Pacesetter	31 (13%)	29 (13%)	60 (13%)	-0.4% [-6.5%, 5.7%]
PSI	4 (2%)	2 (1%)	6 (1%)	
Telectronics	81 (33%)	72 (33%)	153 (33%)	0.6% [-7.9%, 9.2%]
Unknown	8 (3%)	5 (2%)	13 (3%)	1.0% [-2.0%, 4.0%]
Locking Stylet Used	221 (91%)	188 (85%)	409 (88%)	5.5% [-0.5%, 11.5%]
Stylet Reached Distal End of Lead	165 (68%)	146 (66%)	311 (67%)	1.6% [-7.0%, 10.1%]

** Implant duration data missing for 14 LASER and 6 NonLASER removals*

Gender Bias Analysis

Inclusion and exclusion criteria were designed and carried out to avoid gender bias in patient enrollment. Of all patients enrolled, 194 of 301 (64%) were male. This proportion is similar to the 66% male enrollment in the five-years experience with intravascular lead extraction reported

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by Smith, *et al* [2]. The preponderance of males reflects the gender referral pattern for cardiac disease.

Separate analyses of safety and effectiveness data for males and females indicated no differences between the genders; hence, the results presented in the following analyses are representative for both men and women.

10.3 Results

Principal effectiveness and safety results are reported in Table 10-4:

Table 10-4. Principal Effectiveness and Safety Results

	LASER			NonLASER			Difference in
Effectiveness: leads	N	Complete	Partial	Failure	N	Complete	Partial	Failure	Failure[95% CI]
of First Treatment	244	230(94.3%)	6(2.4%)	8(3.3%)	221	142(64.2%)	4(1.9%)	75(33.9%)	-29.8%*[-23%,-36%]
of Crossover Treatments					72	63(87.5%)	3(4.2%)	6(8.3%)	
of Final Treatment	244	230(94.3%)	6(2.4%)	8(3.3%)	221	205(92.8%)	7(3.1%)	9(4.1%)	-0.8%[-2.6%,4.2%]
Total Proc. Time	244	11.2 ± 13.9 min			221	14.7 ± 22.1 min			-3.5*[-6.9,-0.2]

Safety Results: patients	N[a]	LASER		N[b]	NonLASER		Difference
Acute Complications	218	3 (1.4%)	[0.3%, 4.0%]	83	0 (0.0%)	[0.0%, 4.4%]	1.4% [-0.2%,2.9%]
Complications, 1 mo.	218	6 (2.8%)	[1.0%, 5.9%]	83	1 (1.2%)	[0.0%, 6.5%]	1.5% [-1.7%,4.7%]
Death, perioperative	218	1 (0.5%)	[0.0%, 2.5%]	83	0 (0.0%)	[0.0%, 4.4%]	0.5% [-0.3%,1.1%]
Death, 1-mo.	218	2 (0.9%)	[0.1%, 3.3%]	83	1 (1.2%)	[0.0%, 6.5%]	-0.3% [-3.0%,2.4%]

Total Proc. Time (mean ± S.D.) = procedure time for First Treatment + time for Crossover Treatment (if any)

CI = Confidence intervals via normal approximation (Effectiveness) or exact binomial method (Safety)

** = difference statistically significant (p < 0.001) by Chi-Square with continuity correction, or t-test*

[a] includes patients randomized to LASER plus Crossover patients

[b] includes patients randomized to NonLASER less Crossover patients

*Difference = LASER-NonLASER; SEM = sqrt(p1*q1/n1 + p2*q2/n2); 95% CI = Diff ± 1.96*SEM*

A summary of procedure outcomes is shown in Figure 10-2. Analysis of the acute procedural outcome of the first treatment delivered to each lead reveals that the LASER group had a significantly higher success rate (i.e., rate of complete lead extraction) than the NonLASER group (94.3% *vs.* 64.2%, respectively). In the LASER group, 8 (3.3%) leads reached a failure criterion. In the NonLASER group, 75 (33.9%) leads reached a failure criterion. Of these 75 leads, 72 received a second (and final) procedure, using laser tools ("crossover"). Of the 72 crossover procedures, 63 (87.5%) were successful and 6 (8.3%) resulted in failure. The net result for NonLASER leads shows that the final procedure for NonLASER leads (whether it was with nonlaser tools or laser tools) produced 92.8% successes; this is very similar to the LASER outcome (94.3% successes).

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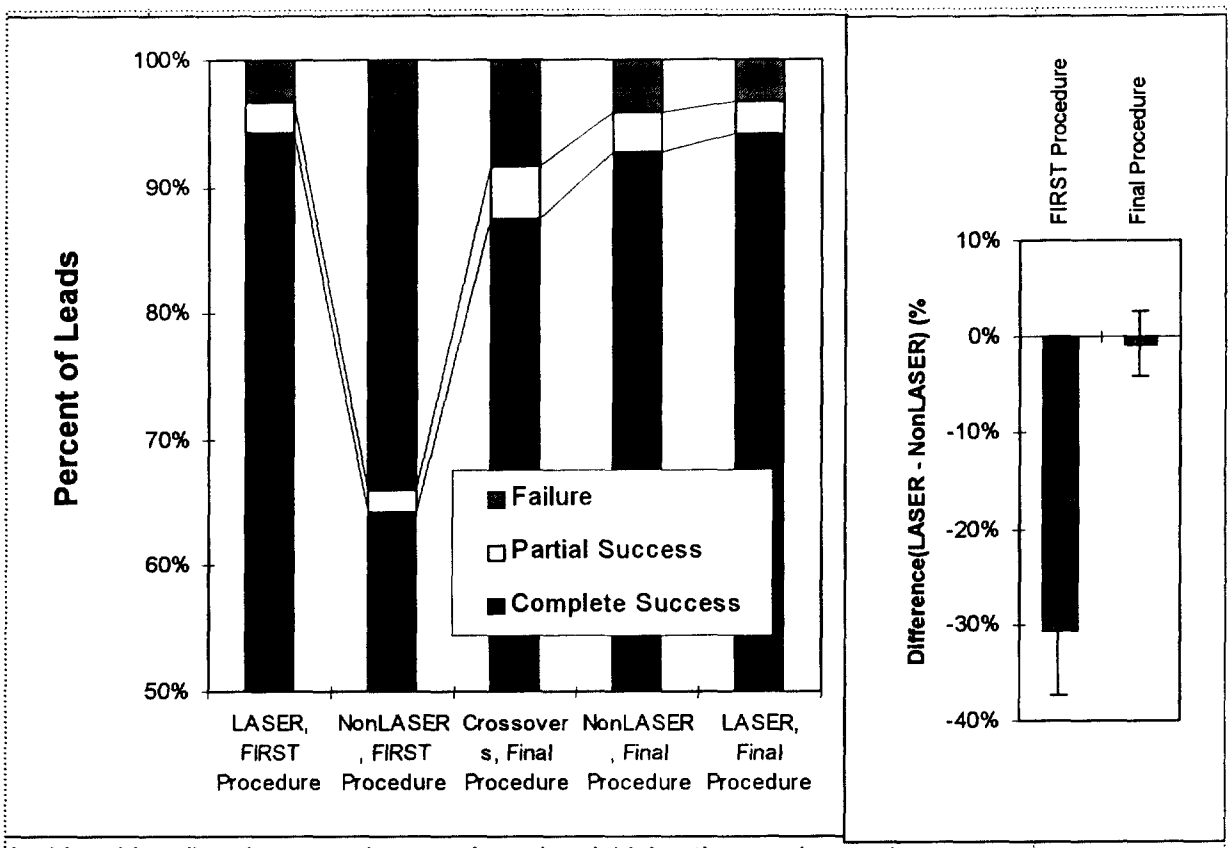
Figure 10-2. Acute Procedure Outcomes

All Patients Randomized (n=301) and All Leads Randomized (n=465)



In this table, all patient groupings are based on initial patient assignments.

	Procedure OUTCOME expressed at % of leads.						
	First Procedure		Cross-over	Final Procedure		First Procedure	Final Procedure
	LASER	NonLaser		LASER	NonLaser	Difference (LASER - NonLASER) [95% CI]	
Failure	8 (3.3%)	75 (33.9%)	6 (8.3%)	8 (3.3%)	9 (4.1%)	-30%*[-36%, -23%]	-0.8% [-4.2%, 2.6%]
Partial	6 (2.4%)	4 (1.9%)	3 (4.2%)	6 (2.4%)	7 (3.1%)	0.0% [-2.4%, 2.4%]	-0.7% [-3.7%, 2.3%]
Success	230 (94.3%)	142 (64.2%)	63 (87.5%)	230 (94.3%)	205 (92.8%)	30%*[23%, 37%]	1.5% [-3.0%, 6.0%]
Total Leads	244	221	72				
Total Patients	153	148	65				

First Procedure : *use of laser tools in the LASER group; use of nonlaser tools only in the NonLASER group*

Final Procedure : *same as First Procedure for LASER group; includes crossover outcomes in NonLASER group*

NonLASER : *randomized to NonLASER group*

LASER : *randomized to LASER group; no crossover possible*

Crossover : *outcome of a laser procedure on leads randomized to NonLASER, on which the NonLASER First Procedure was a failure*

Difference = LASER-NonLASER; SEM = sqrt(pooled SD(1/n_1 + 1/n_2); 95% CI = Diff ± 1.96*SEM*

pooled SD - sqrt((((n_1 - 1)SD_1^2 + (n_2 - 1)*SD_2^2)/(n - 2))*

** = difference statistically significant (p < 0.001) by Chi-Square with continuity correction*

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Correcting for within-patient correlation

Since some patients had more than one lead extracted, the observations of treatment success or failure may not be mutually independent. The usual estimators of the variance for the difference in proportions assume mutual independence of observations. Estimates of p-values and confidence intervals need to assess this dependence and correct for within-patient correlation in the estimates. Table 10-5 shows the number of patients with multiple leads.

Table 10-5. Distribution of patients and leads by cluster size

# Leads/patient	# patients	% patients	# leads	% leads
1	125	41%	125	22%
2	125	41%	250	45%
3	46	15%	138	25%
4	9	2.9%	36	6.5%
7	1	0.33%	7	1.26%
Total	306	100%	556	100%

Generalized Estimating Equations (GEE) provide an approach to estimates for non-independence of repeated measurements[4, 5]. Calculations were done using SUDAAN (release 7.00, Research Triangle Institute, NC). SUDAAN treats individual patients with multiple observations as clusters, as might be done in a sample survey. Table 10-6 summarizes analyses with and without correction for within-patient correlation using the first treatment. The first two rows (Binary) compare complete success to partial success or failure. The GEE correction permits calculation of an odds ratio using proportional odds model that combines Complete Success *vs.* Partial or Failure, plus Partial *vs.* Failure (3 level - GEE corrected)

When a NonLASER extraction failed, the patient was crossed over to laser, and any remaining leads were extracted using the laser. Treatment was thus not "randomly" assigned for these leads (N=91) and they were excluded from the analyses described in Table 10-6.

Table 10-6. Success of Laser vs. Non-laser Lead Removal

All leads randomly assigned for removal (N=465) in 301 patients, excludes post crossover leads (N=91)

Analysis	Difference [95% CI]	Odds ratio [95% CI]
Binary - Uncorrected	30%* [23%, 37%]	9.1* [5.0, 17.0]
Binary - GEE corrected	30%* [22%, 38%]	9.1* [4.7, 17.6]
3 level - GEE corrected		9.4* [4.7, 18.0]

Difference = Success (laser) - Success (non-laser)

Odds ratio = Success (laser) / Success (non-laser), OR > 1 favors laser removal

CI = confidence interval

" = statistically significant (p<0.001) by t-test."*

Correction for within-patient correlation had little impact on the confidence intervals in these comparisons. The ability to generate a single odds ratio for a three-level result is an appealing feature of the GEE approach. The lack of impact of this correction probably reflects both the low within-patient correlation (relative independence) and the large magnitude of difference in

extraction success of laser tool compared to nonlaser tools.

Table 10-7 shows total procedure time and a break-down by first and second procedure for crossovers and by outcome category. Note that total procedure time for NonLASER leads is inclusive (NonLASER + LASER) on an intent-to-treat basis.

Table 10-7. Procedure Times

All Patients Randomized (n=301) and All Leads Randomized (n=465)

TOTAL Procedure Time (minutes)

	LASER				NonLASER			
N	244				221			
Median	7				8			
Range	(0, 95)				(0, 180)			
Mean + SD	11.2 ± 13.9				14.7 ± 22.1			
Diff. [95%CI]	-3.5* [-6.9, -0.2]							
	LASER				NonLASER			
	Complete	Partial	Failure	Total	Complete	Partial	Failure	Total
N	230	6	8	244	205	7	9	221
Mean ± SD	10.1 ± 11.5	15.2 ± 9.4	43.7 ± 35.1	11.2 ± 13.9	12.9 ± 19.2	51.9 ± 45.9	27.2 ± 33.6	14.7 ± 22.1
(range)	(0, 80)	(6, 30)	(5, 95)	(0, 95)	(0, 180)	(11, 120)	(3, 90)	(0, 180)

FIRST Procedure Time (minutes)

	LASER				NonLASER			
	Complete	Partial	Failure	Total	Complete	Partial	Failure	Total
N	230	6	8	244	142	4	75	221
Mean ± SD	10.1 ± 11.5	15.2 ± 9.4	43.7 ± 35.1	11.2 ± 13.9	8.1 ± 9.3	44.8 ± 47.9	13.5 ± 20.9	10.4 ± 15.7
(range)	(0, 80)	(6, 30)	(5, 95)	(0, 95)	(0, 60)	(11, 115)	(0, 120)	(0, 120)
	LASER				NonLASER (CROSSOVERS)			
	Complete	Partial	Failure	Total	Complete	Partial	Failure	Total
N	0	0	0	0	0	0	72	72
Mean ± SD							13.9 ± 21.2	13.9 ± 21.2
(range)							(1, 120)	(1, 120)

SECOND Procedure Time (minutes)

	LASER				NonLASER (CROSSOVERS)			
	Complete	Partial	Failure	Total	Complete	Partial	Failure	Total
N	0	0	0	0	63	3	6	72
Mean ± SD					14.1 ± 15.1	32.3 ± 24.0	23.9 ± 16.1	15.6 ± 15.9
(range)					(1, 63)	(17, 60)	(7, 45)	(1, 63)

Procedure time: wall-clock time, starting from the moment sheaths are applied to attainment of an endpoint

** difference statistically significant by t-test*

11. CONCLUSIONS DRAWN FROM STUDIES

The preclinical testing information and the results of the randomized clinical trial of the 12 Fr. Laser Sheath (PLEXES Trial) provide valid scientific evidence and reasonable assurance that the Spectranetics 12 Fr. Laser Sheath is safe and effective when used in accordance with its labeling.

The safety of the Laser Sheath has been demonstrated by the fact that the incidence of acute complications, complications at 1-month follow-up, perioperative death, and death at 1-month follow-up are comparable for the LASER and nonLASER arms of the PLEXES Trial. The

effectiveness of the device is evident in the significantly higher rate of successful complete lead extractions in the LASER arm (94%) versus the nonLASER arm (64%).

12. PANEL RECOMMENDATIONS

On July 29, 1997, the Circulatory System Devices Panel recommended that Spectranetics' PMA for the 12 Fr. Laser Sheath Kit be approved subject to specific modifications to the labeling. The panel also recommended that a post-approval study be conducted to examine the incidence of complications and death associated with the first ten cases of Laser Sheath use at each new site.

13. FDA DECISION

FDA concurred with the Circulatory System Devices Panel's recommendation of July 29, 1997, and issued a letter to Spectranetics on September 19, 1997, advising that its PMA was approvable subject to specific labeling changes and to their agreement to conduct a post-approval study as recommended by the Panel and required by FDA. The approvable letter also required that the applicant submit information to address other outstanding issues, including those regarding the sterilization, packaging and shelf life of the device. The requirements for the post-approval study of the 12 Fr. Laser Sheath were outlined in the letter as follows:

> A post-approval study of the initial clinical experience of the 12 Fr. Laser Sheath should be conducted. The study should be conducted at all sites where the device is used upon PMA approval and include data on the first ten patients treated at each site. The data collected for each patient should be similar to those collected during the clinical trial of the Laser Sheath (e.g., patient and lead demographical information, indications for lead removal, acute procedural outcome data). These data will be used to determine the "learning curve" of device use by physicians who may not be experienced in lead extraction techniques and whether revisions to the physician training requirements need to be made. The study should continue for two years after PMA approval. Periodic reports of this information should be submitted to the PMA at 6-month intervals.

In PMA amendments received by FDA on September 24 and 29, and December 9, 1997, the applicant addressed all of the items cited in the approvable letter of September 19, 1997. FDA issued an approval order on December 9, 1997. FDA performed an inspection and found the applicant in compliance with the Good Manufacturing Practices (GMP) regulation (21 CFR, Part 820).

This PMA was granted an expedited review on December 23, 1996, because FDA believed that the 12 Fr. Laser Sheath may provide a significant advance in safety over existing clinical techniques for pacing lead extraction and may also benefit public health by aiding in the extraction of pacing leads which have failed and require removal.

14. APPROVAL SPECIFICATIONS

Directions for use: See the attached final draft labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the attached final draft labeling.

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Post-approval Requirements and Restrictions: See approval order.

15. REFERENCES

1. Fearnot NE, et al. Intrasvascular lead extraction using locking stylets, sheaths, and other techniques. PACE 1990; 13:1864-1870.
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4. Liang K, Zeger S: Longitudinal data analysis using generalized linear models. Biometrika 1986;73: 13-22.
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Spectranetics

12 Fr. Laser Sheath Kit

Instructions For Use

Table of Contents

Federal (USA) law restricts this device to sale by or on the order of a physician with appropriate training.

1. Description

The Spectranetics 12 Fr. Laser Sheath Kit includes a 12 Fr. Laser Sheath and a Fish Tape. The Laser Sheath is an intra-operative device used to free a chronically implanted pacing or defibrillator lead.

The laser sheath consists of optical fibers arranged in a circle, sandwiched between inner and outer polymer tubing. The fibers terminate at the distal end within a polished tip and at the proximal end within the coupler that mates with the excimer laser system. At the distal tip, the fibers are protected by inner and outer stainless steel bands, which form a radiopaque marker. The inner lumen of the device is designed to allow a pacing lead to pass through it, as the device slides over the lead towards the tip of the lead in the heart

The laser sheath is designed for use only with the Spectranetics CVX-300® Excimer Laser System. The multifiber laser sheaths transmit ultraviolet energy from the Spectranetics CVX-300® laser to the tissue at the distal tip of the device. When the laser fires, a small amount of the tissue is ablated, thereby freeing the lead from overgrowth in a controllable fashion.

The laser sheath is used in conjunction with conventional lead extraction tools (e.g., locking stylets, outer sheaths).

The Fish Tape is an accessory to assist in the loading of the laser sheath over an implanted lead. The Fish Tape is a 60 cm long, 0.024" diameter, stainless steel mandrel with a wire loop handle on one end and a closed wire hook on the other end.

2. Indications for Use

The laser sheath is intended for use as an adjunct to conventional lead extraction tools in patients suitable for transvenous removal of chronically implanted pacing or defibrillator leads constructed with silicone or polyurethane outer insulation.

3. Contraindications

Use of the Laser Sheath is contraindicated:

- When emergency thoracotomy with cardiopulmonary bypass can not be performed immediately in the event of a life threatening complication;
- When fluoroscopy is not available;
- In patients in whom superior venous approach cannot be used;
- When the proximal end of the pacing lead is not accessible to the operator;
- When the lead will not fit into the inner lumen of the laser sheath.

4. Warnings

Do not attempt to operate the Laser Sheath without the use of conventional lead extraction tools.

The Laser Sheath should be used only by physicians who are experienced In pacing lead removal techniques using telescoping dilator sheaths. The CVX-300® Excimer Laser System should be used only by physicians who have received adequate training (See INDIVIDUALIZATION OF TREATMENT).

Protective glasses are required when the laser is in use. Avoid eye or skin exposure to direct or scattered radiation. Refer to exposure label on the CVX-300® Excimer Laser System.

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Do not insert more than one Laser Sheath or Outer Sheath into a vein at a time. Severe vessel damage, including venous wall laceration requiring surgical repair, may occur.

Lead removal devices should be used only at institutions with emergency cardiac surgical capabilities.

Do not place the outer sheath tip at the SVC-atrial junction as it may damage this delicate area during subsequent procedures, e.g., moving the outer sheath, implanting a new lead.

Maintain appropriate traction on the lead being extracted during advancement of the laser sheath or outer sheath.

When marked calcification that moves with the lead to be extracted is seen on fluoroscopy, particularly in the atrium, the availability of immediate surgical assistance is paramount if a problem presents itself as a result of the extraction procedure. Also, an indication for thoracotomy removal of the lead(s) should be considered.

Do not advance the laser sheath any closer than 1 cm from the lead tip. Do not lase at the myocardium to free the lead tip.

5. Precautions

Thoroughly review the package insert for conventional lead extraction tools before attempting to use the Laser Sheath.

For single use only. Do not resterilize and/or reuse.

Do not use the Laser Sheath:

- If the tamper-evident seal is broken;
- If the Laser Sheath has been damaged.

When the laser sheath is in the body, it should be manipulated only under fluoroscopic observation with radiographic equipment that provides high quality images.

6. Adverse Events

Patients with indications for lead removal (N=301) and with the targeted lead implanted at least one year prior, were randomly assigned into the LASER and NonLASER groups in nine US centers. These 301 patients (465 leads) form the basis for the adverse events reporting.

6.1 Observed Adverse Events

Table 1. Acute Complications and Complications at 1-month All Randomized Patients (n=301)

	LASER	(N=153)	Non-LASER	(N=148)	TOTAL	(N=301)
Complications – Acute	**n**	**%**	**n**	**%**	**n**	**%**
Perioperative Death	1	0.65%	0	0	1	0.3%
Hemopericardium tamponade	2	1.3%	0	0	2	0.7%
Hemothorax	1	0.65%	0	0	1	0.3%
Complications – One Month	**LASER**	**(N=145)**	**Non-LASER**	**(N=140)**	**TOTAL**	**(N=285)**
Death	2	1.4%	1	0.7%	3	1.1%
Complications – any	4	2.8%	3	2.1%	7	2.5%
Pain at cut-down site	1	0.7%	0	0.0%	1	0.4%
Arm swelling	1	0.7%	1	0.7%	2	0.7%
Infection	1	0.7%	1	0.7%	2	0.7%
SVC thrombosis	0	0.0%	1	0.7%	1	0.4%
Tricuspid regurgitation	1	0.7%	0	0.0%	1	0.4%

6.2 Potential Adverse Events

The following adverse events or conditions may also occur during lead extraction with the Laser Sheath, but were not observed during the clinical study (listed in alphabetical order):

- bacteremia
- low cardiac output
- migration of lead fragments
- migration of vegetation
- myocardial avulsion
- perforation
- premature ventricular contractions
- pulmonary embolism
- stroke
- venous avulsion
- ventricular tachycardia

7. Clinical Study

Purpose: The use of standard tools (NonLASER) only (locking stylets, polymer and stainless steel sheaths, grips, snares, etc.) to explant chronically implanted pacing and defibrillator leads was compared to standard tools plus the 12 Fr laser sheath (LASER). The primary effectiveness measure was the proportion of complete extractions (per lead basis). The primary safety measure was complication rate (per patient basis).

Methods: Patients with mandatory or necessary indications for lead removal and with the targeted lead implanted at least one year prior were randomized into the LASER or NonLASER groups in nine US centers between 11/95 and 10/96. The primary endpoint was

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reached if the lead was completely explanted. If the lead fractured, leaving the tip and possibly a portion of the conductor in the patient, the removal was judged a "partial success." The extraction was judged a procedural failure if any of five events occurred: change to femoral or transatrial approach, failure to gain venous entry, failure of sheaths to pass a binding site, lead breakage, or onset of complication. A crossover from NonLASER tools to laser tools was allowed after failure. Crossover patients were analyzed separately. Procedure time, defined as wall-clock time from the moment sheaths were applied until an endpoint was reached, was also recorded.

Description of Patients: 365 patients were enrolled. Five patients were found to meet exclusion criteria after enrollment and were disqualified from the study before any treatment was administered; thus 360 patients were treated. 59 nonrandomized patients were enrolled for investigator training. The remaining 301 patients (with 465 leads) presented with mandatory or necessary indications for lead removal. Mean patient age was 65 years (range 4 to 94) with 36% females and mean implant duration of 67 months (range 1 to 286). Patient characteristics were similar between the two randomized groups.

Results:

Table 2. Principal Effectiveness and Safety Results

	LASER				NonLASER			Difference in	
Effectiveness: leads	N	Complete	Partial	Failure	N	Complete	Partial	Failure	Failure[95% CI]
of First Treatment	244	230(94.3%)	6(2.4%)	8(3.3%)	221	142(64.2%)	4(1.9%)	75(33.9%)	-29.8%*[-23%,-36%]
of Crossover Treatments					72	63(87.5%)	3(4.2%)	6(8.3%)	
of Final Treatment	244	230(94.3%)	6(2.4%)	8(3.3%)	221	205(92.8%)	7(3.1%)	9(4.1%)	-0.8%[-2.6%,4.2%]
Total Proc. Time	244	11.2	±13.9 min		221	14.2	±21.6 min		-3.05*[-3.12,-2.97]

Safety Results: patients	N[a]	LASER	N[b]	NonLASER	Difference
Acute Complications	218	3 (1.4%) [0.3%, 4.0%]	83	0 (0.0%) [0.0%, 4.4%]	1.4% [-0.2%,2.9%]
Complications, 1 mo.	218	6 (2.8%) [1.0%, 5.9%]	83	1 (1.2%) [0.0%, 6.5%]	1.5% [-1.7%,4.7%]
Death, perioperative	218	1 (0.5%) [0.0%, 2.5%]	83	0 (0.0%) [0.0%, 4.4%]	0.5% [-0.3%,1.1%]
Death, 1-mo.	218	2 (0.9%) [0.1%, 3.3%]	83	1 (1.2%) [0.0%, 6.5%]	-0.3% [-3.0%,2.4%]

Total Proc. Time (mean ± s.d.) = procedure time for First Treatment + time for Crossover Treatment (if any)
CI = Confidence intervals via binomial approximation (Effectiveness) or exact binomial method (Safety)
* = difference statistically significant ($p < 0.001$) by Chi-Square with continuity correction, or t-test
[a] includes patients randomized to LASER plus Crossover patients
[b] includes patients randomized to NonLASER less Crossover patients
Difference = LASER-NonLASER; SEM = sqrt(p1*q1/n1 + p2*q2/n2); 95% CI = Diff ± 1.96*SEM

8. Individualization of Treatment

Weigh the relative risks and benefits of intravascular catheter/lead removal procedures in cases when:

- The lead to be removed has a sharp bend or evidence of fracture;
- The lead shows evidence of insulation disintegration raising the concern of pulmonary embolism;
- Vegetations are attached directly to the lead body.

When an outer sheath, used in conjunction with the Laser Sheath during the lead extraction procedure, is left in place once the Laser Sheath and lead are removed from the patient, the outer sheath may then be used as a conduit for a guidewire to facilitate the implantation of a new lead.

The outer sheath tip should be either (a) fully into the atrium, or (b) retracted into the brachiocephalic vein. Placing the outer sheath tip at the SVC-atrial junction risks damage to this delicate area during subsequent procedures, such as moving the outer sheath or implanting a new lead and is thus not recommended.

It is vital that appropriate traction be maintained on the lead being extracted both during laser assisted and standard extraction attempts. If appropriate levels of traction cannot be maintained on the lead in order to offset the counter-pressures that distort the lead body, then changing to an alternative extraction methodology such as the femoral approach would be indicated.

When marked calcification that moves with the lead to be extracted is seen on fluoroscopy, particularly in the atrium, the availability of immediate surgical assistance is paramount if a problem presents itself because of the extraction procedure. Also, an indication for thoracotomy removal of the lead(s) should be considered.

The safety and effectiveness of the Laser Sheath has not been established in patients with the following conditions.

- Recent history of pulmonary embolus
- Leads implanted in the coronary sinus

9. Operator's Manual

9.1 Sterilization

For single use only. Do not re-sterilize and/or reuse.

The Spectranetics laser sheaths are supplied sterile. Sterility is guaranteed only if the package is unopened and undamaged.

9.2 Inspection Prior to Use

Before use, visually inspect the sterile package to ensure that seals have not been broken. All equipment to be used for the procedure, including the laser sheath, should be examined carefully for defects. Examine the laser sheath for bends, kinks or other damage. Do not use if it is damaged.

9.3 Procedure Set Up

Laser Sheath preparations:

1. Using sterile technique, open the sterile package. Remove the packaging wedges from the tray and gently lift the device from the tray while supporting the proximal coupler.

2. Connect the proximal end of the device to the connector of the CVX-300®

3. Calibrate the Laser Sheath following the instructions in the "Operational Modes" section of the CVX-300® Operator's Manual (7030-0035 or 7030-0006), with the following exception: set calibration fluence to 60 MJ/mm^2 and repetition rate to 40 Hz.

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Patient preparations:

1. Obtain a thorough patient history, including patient blood type. Appropriate blood products should be readily available.
2. Ascertain the manufacturer, model number and implant date of the catheter/lead to be removed. Perform radiographic/echocardiographic evaluation of catheter/lead condition, type and position.
3. Use a procedure room that has high quality fluoroscopy, pacing equipment, defibrillator, and thoracotomy and pericardiocentesis trays.
4. Prep and drape the patient's chest for possible thoracotomy; prep and drape the patient's groin for a possible femoral approach extraction procedure.
5. Establish back-up pacing as needed.
6. Have available additional Laser Sheaths, Outer Sheaths, locking stylets, stylets to unscrew active fixation leads, snares (femoral workstation) and any other accessory equipment deemed necessary.

9.4 Compatibility of Laser Sheath and Pacemaker/ICD) Lead

The table below shows the dimensional compatibility between the 12 Fr. Laser Sheath, the Pacemaker/ICD Lead to be removed and the Outer Sheath. It is vital that the physician determines the maximum outside diameter (OD) of the lead before extraction with the laser sheath is attempted. This information should be obtained from the lead manufacturer.

12 Fr. Laser Sheath:	ID = Inside Diameter OD = Outside Diameter
Model #	**500-001**
Minimum Tip ID, in. / Fr	.109 / 8.3
Maximum Tip OD, in. / Fr	.163 / 12.4
Lead: Maximum OD, Fr	7.5
Outer Sheath: Minimum ID, Fr	13

9.5 Clinical Technique

1. Patients prepared for lead extractions are prepared for multiple approaches, including an emergency cardiac surgical procedure. Preparations may include: general endotracheal anesthesia or conscious sedation, shave and preparation of both the chest and groin areas, ECG monitoring, insertion of an arterial line and a Foley catheter, presence of instruments for pacing and defibrillation, an electrosurgical unit, and a sternal saw for emergencies.

2. A temporary pacing lead is inserted in all patients needing a pacemaker. An exception is made for patients with an implanted permanent pacemaker whose leads are not to be extracted.

3. Fluoroscopy will be used to monitor all transvenous maneuvers.

4. Expose the proximal end of the lead. Debride overgrowth from the lead as required to expose the venous entry site. Sever the lead connector and remove the anchoring sleeve.

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5. Insert and lock a locking stylet into the lead. Alternatively, a length of suture material approximately 60 cm long may be attached to the proximal end of the lead to act as a traction device.

6. Fill a sterile syringe with 10 cc of saline solution. Inject the saline into the inner lumen of the Laser Sheath. Using another 10 cc of saline, moisten the outer jacket of the laser sheath.

7. Place an outer sheath over the laser sheath.

8. Using a "Fish Tape" device, thread the handle of the traction device through the inner lumen of the Laser Sheath. Remove the "Fish Tape" after the traction device handle emerges from the proximal end of the laser sheath. Thread the proximal end of the lead into the inner lumen of the laser sheath.

9. Extraction technique:

   a. Using an "inchworm" technique, alternately advance the outer sheath and the laser sheath over the lead.

   b. Use the following guidelines to determine if a tissue obstruction is met:

      - The laser sheath will not advance into the vein.
      - The laser sheath bows outward slightly when longitudinal pressure is applied.
      - Fluoroscopy shows that the sheath tip does not advance relative to the lead body
      - Fluoroscopy shows that the laser sheath tip is not caught on a lead electrode, a lead bend, or another lead.

   c. When an obstruction is met and the laser sheath cannot be advanced:

      - Use orthogonal fluoroscopic views to ensure that the tip of the laser sheath is aligned with the longitudinal axis of the lead.

      - Retract the outer sheath so that its distal end does not overlap the tip of the Laser Sheath. Press the laser sheath gently into the obstructing tissue.

      - Place the laser in READY mode. Depress the foot switch, activating the laser. While the laser is firing, use gentle pressure on the laser sheath to advance the device approximately 1 mm per second while applying equal and opposite traction to the traction device. If the laser sheath breaks through the obstruction during lasing, release the foot switch.

      NOTE: Advancing the laser sheath through moderately calcified tissue may require more pulses of laser energy than through fibrous scar overgrowth.

      - Advance the outer sheath to the new position of the laser sheath.

   d. If the traction device unlocks its grip on the lead, it is necessary to remove the laser sheath and outer sheath, and apply a new traction device, before proceeding again with the laser sheath.

e. Advance the outer sheath and laser sheath to the desired location on the lead, as described in 9 (a-c) above. Do not advance the laser sheath any closer than 1 cm from the lead tip. Do not lase at the myocardium to free the lead tip.

f. If necessary, use countertraction, using the outer sheath and the traction device, to free the lead tip from the heart wall.

10. Withdrawal of the laser sheath and outer sheath can be accomplished at any time during the procedure. If the lead is free, it should be drawn into the laser sheath before the lead, the laser sheath, and the outer sheath are removed from the body.

NOTE: If the laser sheath is removed from the body for any reason, thoroughly clean the device shaft and tip with saline to prevent blood from sticking.

9.6 Physician Training

Physician training in use of the Laser Sheath and CVX-300® Excimer Laser System should include:

- Classroom training in laser safety and physics;
- A videotape review of laser operation followed by a demonstration of the CVX-300® Excimer Laser System;
- Hands-on training in the use of the CVX-300 Excimer Laser System in lead removal;
- Observation of the removal of at least two leads with the Laser Sheath performed by an experienced Laser Sheath user;
- Removal of at least two leads in the presence of a second physician experienced in lead removal techniques and a fully trained Spectranetics representative.

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